## HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 1 of 8 Title: METHODS FOR THE PRODUCTION OF REDOX PROTEINS. Applicant: van Rooijen et al. Serial No. 10/032,201 Filed: December 19, 2001 Our Docket No.: 38814-351B

	60
TR ATGAATGGTCTCGAAACTCACAACACAAGGCTCTGTATCGTAGGAAGTGGCCCAGCGGCATTHIREDBATGAATGGTCTCGAAACTCACAAAGGCTCTGTATCGTAGGAAGTGGCCCAGCGGC	
ALLE CONTROL OF A	<u> </u>
70 80 90 100 110 17 TR CACACGGCGGCGATTTACGCAGCTAGGGCTGAACTTAAACCTCTTCTCTTCGAAGGATG	20
ATTHIREDS CACACGGCGGCGATTTACGCAGCTAGGGCTGAACTTAAACCTCTTCTCTTCGAAGGATG	
130 140 150 160 170 18	80
TR ATGGCTAACGACATCGCTCCCGGTGGTCAACTAACCACCACCACCGACGTCGACAATTT	C
ATTHIREDB A T G G C T A A C G A C A T C G C T C C C G G T G G T C A A C T C A A C C A A C C C G C G T - G A G A A T T T	의
	40
TR CCCGGATTTCCAGAAGGTATTCTCGGAGTAGAGCTCACTGACAAATTCCGTAAACAATC	
Z50 Z60 Z70 Z80 Z90 3C TR GAGCGATTCGGTACTACGATATTTACAGAGACGGTGACGAAAGTCGATTTCTCTTCGAA	
ATTHIREDB G A G C G A T T C G G T A C T A C G A T A T T T A C A G A G A C G G T G A C G A A A G T C G A T T T C T C T T C G A A	
310 320 330 340 350 36	60
TR CCGTTTAAGCTATTCACAGATTCAAAAGCCATTCTCGCTGACGCTGTGATTCTCGCTAC	
ATTHIREDB C C G T T T A A G C T A T T C A C A G A T T C A A A A G C C A T T C T C G C T G A C G C T G T G A T T C T C G C T A T	C
	20
TR GGAGCTGTGGCTAAGCGGCTTAGCTTCGTTGGATCTGGTGAAGGTTCTGGAGGTTTCTG ATTHIREDBGGAGCTGTGGCTAAGTGGCTTAGCTTCGTTGGATCTGGTGAAGTTCTCGGAGGTTTCTG	
430 440 450 460 470 48 TR ACCGTGGAATCTCCGCTTGTGCTGTTTGCGACGGAGCTGCTCCGATATTCCGTAACAA	A)
ATTHIREDB A A C C G T G G A A T C T C C G C T T G T G C T G T T T G C G A C G G A G C T G C T C C G A T A T T C C G C A A C A A	
490 500 510 520 530 54	40
TR CCTCTTGCGGTGATCGGTGGAGGCGATTCAGCAATGGAAGAAGCAAACTTTCTTACAAA	A
ATTHIREDB C C T C T T G C G G T G A T C G G T G G A G G C G A T T C)T G C A A T G G A A G C A A A C T T T C T T A C A A A	A
	00
TR TATGGATCTAAAGTGTATATAATCCATAGGAGAGATGCTTTTAGAGCGTCTAAGATTAT ATTHIREDB TATGGATCTAAAGTGTATATAATCGATAGGAGAGATGCTTTTAGAGCGTCTAAGATTAT	G
610 620 630 640 650 660 TR CAGCAGCGAGCTTTGTCTAATCCTAAGATTGATGTGATTTGGAACTCGTCTGTTGTGGA	<u>60</u>
ATTHIREDB C A G C A G C G A G C T T T G T C T A A T C C T A A G A T T G A T T T G G A A C T C G T C T G T G T G G A	A
670 680 690 700 710 72	20
TR GCTTATGGAGAAAGAGATGTGCTTGGAGGATTGAAAGTGAAGAATGTGGTAC	C
ATTHIREDB G C T T A T G G A G A T G G A G A A G A G A	C
	во
TR GGAGATGTTTCTGATTTAAAAGTTTCTGGATTGTTCTTTGCTATTGGTCATGAGCCAGC ATTHIREDBGGAGATGTTTCTGATTTAAAAGTTTCTTGGATTGTTCTTTGCTATTTGGTCATGAGCCAGC	
ATTAINED G G A G A T G T T T C T G A T T T T T C T G G T C A T G A G C C A G C	<u>ت</u>
790 800 810 820 830 840 TR ACCAAGTTTTGGATGGTGGTGTTTAGATTCGGATGGTTATGTTGTCACGAAGCC	10
ATTHIRED A C C A A G T T T T T G G A T G G T G G T T G A G T T A G A T T C G G A T G G T T A T G T T G T C A C G A A G C C	
850 860 870 880 890 90	 30
TR GGTACTACACAGACTAGCGTTCCCGGAGTTTTCGCTGCGGGTGATGTTCAGGATAAGAA	G)
ATTHIREDB G T A C T A C A C A G A C T A G C G T T C C C G G A G T T T T C G C T G C G G G T G A T G T T C A G G A T A A G A A	G
910 920 930 940 950 96	
TR TATAGGCAAGCCATCACTGCTGCAGGAACTGGGTGCATGGCAGCTTTGGATGCAGAGCA	
ATTHIREDB T A T A G G C A A G C C A T C A C T G C T G C A G G A A C T G G G T G C A T G G C A G C T T T G G A T G C A G A G C A	T
970 980 990 1000 1010 102 TR TACAAGAGATTGGATCTCAGCAAGGTGATTGA	20
TR TACTTACAAGAGATTGGATCTCAGCAAGGTAAGAGTGATTGA ATTHIREDB TACTTACAAGAGATTGGATCTCAGCAAGGTAAGAGTGATTGA	

FIG. I

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Translation of ATTHIREDB M N G L I Translation of TR	10 ETHNTRLCIVGSGP ETHNTRLCIVGSGP	20 PAAHTAAIYAA PAAHTAAIYAA	30 RAELKPLLF RAELKPLLF	40 EGWMANDIA EGWMANDIA	PGGQLNQPP-RENF PGGQLTTTTDVENF
Translation of ATTHIREDB P G F P I	70 EGILGVELTDKFRK EGILGVELTDKFRK	80 < Q S E R F G T T I F < Q S E R F G T T I F	90 TETVTKVDF TETVTKVDF	SSKPFKLFT SSKPFKLFT SSKPFKLFT	110 DSKAILADAVILA DSKAILADAVILA T
Translation of ATTHIREDB G A V A I Translation of TR	X W L S F V G S G E V L G K R L S F V G S G E G S G	140 GLWNRGISACA GFWNRGISACA	150 V C D G A A P I F V C D G A A P I F	160 RNKPLAVIG RNKPLAVIG	GGDSAMEEANFLTK GGDSAMEEANFLTK
Translation of ATTHIREDB Y G S K V Y Translation of TR	I I D R R D A F R A S I I H R R D A F R A S	X I M Q Q R A L S N P K I M Q Q R A L S N P	K I D V I W N S S K I D V I W N S S	VYEAYGDGE VYEAYGDGE	240 R D V L G G L K V K N V V T R D V L G G L K V K N V V T
Translation of ATTHIREDB G D V S Translation of TR	250 DLKVSGLFFAIGHE DLKVSGLFFAIGHE	EPATKFLDGGVEPATKFLDGGV	ELDSDGYVV ELDSDGYVV	Z80 TKPGTTQTS TKPGTTQTS	290 V P G V F A A G D V Q D K K V P G V F A A G D V Q D K K
Translation of ATTHIREDB Y R Q A I T A Translation of TR	310 AGTGCMAALD AGTGCMAALD	320 AEHYLQEIGSQ AEHYLQEIGSQ	330 Q G K S D Q G K S D	340	350 360

Calles their their series to =

40 P L V F E G = T S F P L L F E G M M A N D I A P 90 G A E L R T E D V E S V S L G A T E T E T V T E V D F	140 E = = = E E E E E E E E E E E E E E E E	X V Y L L H R R D A F R 240  R L R N T T G E E T T K V K N V V T G D V S D	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	TTEETGDVDSTDTT TTEETGDVDSTDTT	$\frac{290}{E} = \frac{V}{E} = \frac{V}{L} = \frac{V}{V} = \frac{V}{V} = \frac{W}{V} = $	A40 REFQVSIPTMILF SDWAIQAMPTEMFL	490 500 FIG. 3
ł I I	110 120 130 130 170 170 170 170 170 170 170 170 170 180 170 170 180 180 170 170 180 180 180 180 180 180 180 180 180 18	A V C D G A A P I F R N K P L A V I G G D S A M E E A N F L T K Y G S S A M E E A N F L T K Y G S S S S S S 10 K I M D K I K I M N D K I M N D K I M N D K I M N S S V V E A Y G D G E R D V L G G L K I M Q Q R A L S N P K I D V I W N S S V V E A Y G D G E R D V L G G L		1			M. lep $TR/Trxh$ $Q G Q Q P V R R I V G A K G K A A L L R D L S D V V P N L N A R A R A R A R A R A R A R A R A R A$

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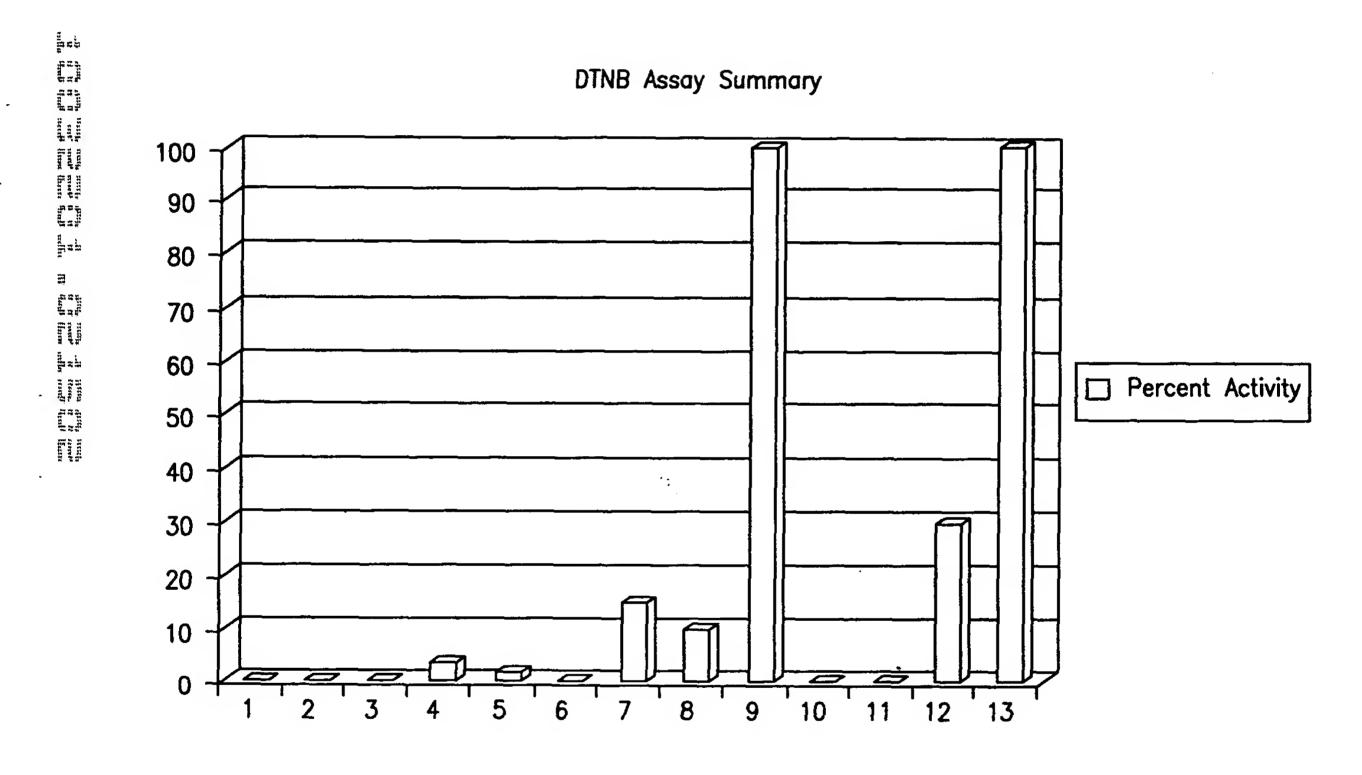


FIG. 4

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## **HETEROMULTIMERS**

Class	Heteromultimer	Example sequence reference for			
		heteromultimeric subunits			
Biosynthetic	3-methyl-2-oxobutanoate	McKean, et al. Biochim. Biophys. Acta (1992)			
	dehydrogenase (2-oxoisovalerate	1171:109-112 / Chuang, J.L., et al FEBS Lett. a			
dehydrogenase (lipoamide))- E1		(1990) 262 (2), 305-309.			
	component)				
Biosynthetic	3-oxoadipate CoA-transferase	Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992)			
		174:4657-4666			
Biosynthetic	anthranilate synthase:indole-3-glycerol	Zalkin, H.; et al. J. Biol. Chem. (1984) 259:3985-			
	phosphate synthase	3992.			
Biosynthetic	beta-ketoacyl-[acyl carrier protein]	Siggaard-Andersen, M. et al. Proc. Natl. Acad. Sci.			
	synthase I	U.S.A. (1991) 88:4114-4118			
Biosynthetic	butyrateacetoacetate CoA-transferase	Fischer, R.J., et al. J. Bacteriol. (1993) 175 (21),			
		6959-6969.			
Biosynthetic	cAMP dependent protein kinase	Mutzel, R et al. Proc. Natl. Acad. Sci. U.S.A. (1987)			
	-	84:6-10./ Burki, E., et al. Gene (1991) 102 (1), 57-			
		65.			
Biosynthetic	carbamoyl-phosphate synthase	Shigenobu, S., et al. Nature. (2000) 407 (6800), 81-			
•		86.			
Biosynthetic	Creatine kinase	Billadello, J.J.; et al. Biochem. Biophys. Res.			
		Commun. (1986) 138:392-398. / Roman, D.; et al.			
		Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.			
Biosynthetic	gamma-glutamyltransferase (gamma-	Papandrikopoulou, A.; et al. Eur. J. Biochem.			
	glutamyl transpeptidase)	(1989) 183:693-698.			
Biosynthetic	glutathione transferase	Могтоw, C.S. et al. Gene (1989) 75:3-11			
Biosynthetic	glycerol-3-phosphate dehydrogenase	Cole, S.T. et al. J. Bacteriol. (1988) 170:2448-2456.			
Biosynthetic	guanylate cyclase	Hinsch, K.D. et al. FEBS Lett. (1988) 239:29-34/			
•		Koesling, D. et al. FEBS Lett. (1990) 266:128-132.			
Biosynthetic	heterodisulfide reductase	Smith, D.R., et al. J. Bacteriol. (1997) 179 (22),			
	·	7135-7155.			
Biosynthetic	human cathepsin	Ritonja, A. et al. FEBS Lett. (1988) 228:341-345.			
Biosynthetic	Hydrogenase	Menon, N.K. et al. J. Bacteriol. (1990) 172:1969-			
		1977.			
Biosynthetic	Meprin A	Johnson, G.D. and Hersh, L.B. J. Biol. Chem.			
		(1992) 267:13505-13512.			
Biosynthetic	methionine adenosyltransferase	Horikawa, S.; Tsukada, K. FEBS Lett. (1992)			
		312:37-41.			
Biosynthetic	methylmalonyl-CoA mutase	Jackson, C.A. et al. Gene (1995) 167:127-132.			
Biosynthetic	mitochondrial processing peptidase	Pollock, R.A. et al. EMBO J. (1988) 7:3493-3500.			
Biosynthetic	Na+/K+-exchanging ATPase	Shull, G.E., et al. Biochemistry (1986) 25 (25),			
		8125-8132./Mercer,R.W., et al.			
		Mol. Cell. Biol. (1986) 6 (11), 3884-3890./			
		Mercer, R.W., et al. J. Cell Biol. (1993) 121 (3),			
		579-586.			
Biosynthetic	NAD(+)-dependent isocitrate	Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem.			
	dehydrogenase	(1992) 267:16417-16423. /Cupp, J.R. and			
		McAlister-Henn, L.			
		J. Biol. Chem. (1991) 266:22199-22205.			
Biosynthetic	phosphoribosylformylglycinamidine	Ebbole, D.J.; Zalkin, H. J. Biol. Chem. (1987)			
	synthase	262:8274-8287.			
Biosynthetic	protocatechuate 3,4-dioxygenase	Frazee, R.W.; et al. J. Bacteriol. (1993) 175:6194-			
	, , , , , , , , , , , , , , , , , , , ,	6202.			
		Engelkamp, D.; et al. Biochemistry (1992)			

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PROTEINS.

	<u> </u>	31:10258-10264. / Allore, R.J.; et al. J. Biol. Chem.		
		(1990) 265:15537-15543.		
Biosynthetic	sucrosefructan 6-fructosyltransferase	Sprenger, N.; et al. Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.		
Biosynthetic	Superoxide dismutase	Capo, C.R.; et al. Biochem. Biophys. Res. Commun. (1990) 173:1186-1193.		
Biosynthetic	Urease	Labigne, A.; et al. J. Bacteriol. (1991) 173:1920- 1931.		
Biosynthetic	urokinase-type plasminogen activator (urokinase)	Belin, D. et al. Eur. J. Biochem. (1985) 148:225-232.		
Biosythetic	methylmalonyl-coenzyme A mutase	Birch, A., et al J. Bacteriol. (1993) 175 (11), 3511-3519.		
Calcium binding	Calcineurin	Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. et al. DNA (1989) 8:675-682.		
Calcium binding	Calgranulin Imamichi, T. et al. Biochem. Biophys. Res. Commun. (1993) 194:819-825.			
Calcium binding	Calpain	Aoki, K. et al. FEBS Lett. (1986) 205:313-317.		
DNA binding	API	van Straaten, F., et al. Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. /Hattori, K., et al Proceedings of the National Academy of Sciences of the United States of America. (1988) 85 (23), 9148-9152.		
DNA binding	сМус-Мах	Schreiber-Agus, N et al. Mol. Cell. Biol. (1993) 13 (5), 2765-2775.		
DNA binding	DNA binding protein HU-1/HU-2	Laine, B. et al. Eur. J. Biochem. (1980) 103:447-461.		
DNA binding	hepatic nuclear factor 1	Bach, I. et al. Nucleic Acids Res. (1992) 20 (16), 4199-4204. / Rey-Campos, J. et al. EMBO J. (1991) 10 (6), 1445-1457.		
DNA binding	Integration host factor	Miller, H.I. Cold Spring Harbor symposia on quantitative biology. (1984) 49, 691-698. / Flamm, E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117-128.		
DNA binding	Ku	Reeves, W.H. and Sthoeger, Z.M. J. Biol. Chem. (1989) 264 (9), 5047-5052. / J. Biol. Chem. (1989) 264 (23), 13407-13411.		
DNA binding	MutS	Bocker et al. 1999. Cancer Research 59, 816-822.		
DNA binding	NF-E2	Chan, J.Y. et al Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370./ Toki, T., et al. Oncogene (1997) 14 (16), 1901-1910.		
DNA binding	nuclear factor kB (NFkB)	Kieran M, et al. Cell. (1990) Sep 7;62(5):1007-18. / Ruben SM, et al. Science (1991) Mar 22;251(5000):1490-3. Erratum in: Science (1991) Oct 4;254(5028):11		
Electron transport	corrinoid/iron-sulfur protein	Lu, W.P. et al. J. Biol. Chem. (1993) 268:5605- 5614.		
Electron transport	cytochrome d ubiquinol oxidase	Green, G.N. et al. J. Biol. Chem. (1988) 263:13138-13143.		
Electron transport	cytochrome-c3 hydrogenase	Мелоп, N.K. et al. J. Bacteriol. (1987) 169:5401- 5407.		
Electron transport	electron transfer flavoprotein	Finocchiaro, G. et al. Biol. Chem. (1988) 263:15773-15780. / Finocchiaro, G. et al. Eur. J. Biochem. (1993) 213:1003-1008.		

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Flaction transport	vulene monoovugenese	Shaw, J.P. and Harayama, S. Eur. J. Biochem.		
Electron transport	xylene monooxygenase	(1992) 209:51-61. / Kasai, Y., et al. J. Bacteriol.		
		(2001) 183 (22), 6662-6666.		
Growth factor	henotogyte grouph factor	Nakamura, T. et al. Nature (1989) 342:440-443.		
	hepatocyte growth factor	<u></u>		
Growth factor	human chorionic gonadotropin	Morgan, F.J. et al. J. Biol. Chem. (1975) 250 (13), 5247-5258.		
Growth factor	Platelet-derived growth factor	Takimoto, Y., et al. Hiroshima J. Med. Sci. (1993)		
		42 (1), 47-52./ Josephs, S.F., et al. Science (1984) 225 (4662), 636-639.		
Hormone	Bombyxin	Adachi, T. et al. J. Biol. Chem. (1989) 264:7681-7685.		
Hormone	Follicle stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.		
		Genet. (1981) 1 (1), 3-18. / Watkins, P.C., et al. DNA (1987) 6 (3), 205-212.		
Hormone	Insulin	Bell, G.I., Pictet, R.L., Rutter, W.J., Cordell, B.,		
		Tischer, E. and Goodman, H.M.		
		Sequence of the human insulin gene. Nature. 284		
		(5751), 26-32 (1980)		
Hormone Luteinizing Hormone		Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.		
		Genet. (1981) 1 (1), 3-18. / Shome, B. and		
		Parlow, A.F. J. Clin. Endocrinol. Metab. (1973) 36		
	·	(3), 618-621.		
Hormone	Thyroid stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.		
		Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, et al.		
		FEBS Lett. (1985) 188 (2), 394-400.		
Immune	B-cell antigen receptor complex	Hashimoto, S. et al. J. Immunol. (1993) 150 (2), 491-		
		498. / Flaswinkel, H. and Reth, M.		
		Immunogenetics (1992) 36 (4), 266-269.		
Immune	Cell surface CD8 molecules	Ureta-Vidal, A., et al. Immunogenetics (1999) 49		
		(7-8), 718-721.		
Immune	human complement subcomponent Clq	Sellar, G.C. et al. Biochem. J. (1991) 274:481-490.  Talken, B.L. et al. Scand. J. Immunol. (2001) 54 (1-		
Immune	T cell receptor	Talken, B.L. et al. Scand. J. Immunol. (2001) 54 (1-2), 204-210.		
Di		Offner, G.D. et al. J. Biol. Chem. (1981) 256:12167-		
Photosynthesis	C-phycocyanin	12175. / Troxler, R.F. et al. J. Biol. Chem. (1981) 256:1216/-		
		256:12176-12184.		
Di		Chow, L.P. et al. Eur. J. Biochem. (1995) 231:149-		
Photosynthesis ferroredoxin-thioredoxin reductase		Chow, L.P. et al. Eur. J. Biochem. (1995) 231:149- 156. / Iwadate, H. et al. Eur. J. Biochem. (1994)		
Photosynthesis	Tichthanastica camplas I	223:465-471.		
Photosynthetic	Light harvesting complex I	Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.  Carrillo, N. et al. Curr Genet. 1986;10(8):619-24.		
Protease	cytochrome b559			
Flotease	ATP-dependent Clp protease	Gerth, U. et al. Gene (1996) 181:77-83. / Kunst,F. et al. Nature (1997) 390 (6657), 249-256.		
Receptor	alpha-2-macroglobulin receptor	Strickland, D.K. et al. J. Biol. Chem. (1990)		
		265:17401-17404. / Strickland, D.K. et al. J. Biol.		
		Chem. (1991) 266:13364-13369.		
Receptor Interleukin-2 receptor		Ishida, N. et al. Nucleic Acids Res. (1985) 13:7579-		
		7589. / Hatakeyama, M. et al. Science (1989)		
		244:551-556 / Takeshita, T. et al. Science (1992)		
		257:379-382.		
Receptor	platelet-derived growth factor receptor	Lee, K.H. et al. Mol. Cell. Biol. (1990) 10:2237-		
		2246. / Herren, B. et al. Biochim. Biophys. Acta		
		1173 (3), 294-302 (1993).		
Structural	Hemoglobin	Heindell, H.C. et al. Cell (1978) 15 (1), 43-54.		

FIG. 5C

		Best, J.S. et al. Hoppe-Seyler's Z. Physiol. Chem. (1989) 350 (5), 563-580. / Hardison, R.C. J. Biol. Chem. (1981) 256 (22), 11780-11786.		
Structural	human platelet glycoprotein Ib	Wenger, R.H. et al. Biochem. Biophys. Res. Commun. (1988) 156 (1), 389-395. / Yagi, M. et al. J. Biol. Chem. (1994) 269 (26), 17424-17427.		
Structural	Plasma fibronectin	Kornblihtt, A.R. et al. Proc. Natl. Acad. Sci. U.S.A. (1983) 80:3218-3222.		
Structural	Spectrin	Sahr, K.E. et al. J. Biol. Chem. (1990) 265:4434-4443. / Winkelmann, J.C. et al. J. Biol. Chem. (1990) 265:11827-11832.		
Structural	Tubulin	Ponstingl, H. et al. Proc. Natl. Acad. Sci. U.S.A. (1981) 78:2757-2761. / Krauhs, E. et al. Proc. Natl. Acad. Sci. U.S.A. (1981) 78:4156-4160.		
Toxin	Agkisacutacin	Cheng, X. et al. Biochem. Biophys. Res. Commun. (1999) 265 (2), 530-535.		
Toxin	Beta bungarotoxins	Kondo, K. et al. J. Biochem. (1978) 83:101-115.		
Toxin	Crotoxin	Bouchier, C. et al. Nucleic Acids Res. (1988) 16 (18), 9050.		
Toxin	Mojave toxin	John, T.R. et al. Gene (1994) 139:229-234.		
Toxin	venom protein C9S3	Rowan, E.G. et al. Nucleic Acids Res. (1990) 18:1639. / Joubert, F.J. and Viljoen, C.C. Hoppe- Seyler's Z. Physiol. Chem. (1979) 360:1075-1090.		
Miscellaneous	Inhibin	Forage, R.G. et al. Proc. Natl. Acad. Sci. U.S.A. (1986) 83:3091-3095.		
Miscellaneous	Monellin	Frank, G. and Zuber, H. Hoppe-Seyler's Z. Physiol. Chem. (1976) 357:585-592.		
Miscellaneous	mRNA capping enzyme	Niles, E.G. et al., J. Virology (1986) 153:96-112.		
Miscellaneous	Soybean insulin-binding protein si30	Barbashov, S.F. et al. Bioorg. Khim. (1991) 17:421-423.		

FIG. 5D